

Clean Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

a | 1. (Amended) A covalently polymerizable, water-absorbing, hydrogel-forming material,
wherein the material has both hydrophilic and hydrophobic regions and is polymerized to form a hydrogel characterized as having the following properties:
a) absorbing water to less than about 300% of its initial weight, on equilibration with water or bodily liquids;
b) having a solids content of at least about 20% after equilibration in water or bodily liquids;
c) having an elongation to failure of at least about 25% hydration to equilibrium; and
d) being sufficiently biocompatible to permit the treatment or repair of biological tissue, or used as an implant in a patient.

2. The material of claim 1, having a molecular weight after polymerization of at least 10 kDa.

3. The material of claim 1, which is covalently crosslinked.

4. The material of claim 1, which is non-covalently crosslinked.

5. The material of claim 1, having a tensile modulus of at least about 50 kPa after equilibrium hydration.

6. The material of claim 1, having an equilibrium water content of at least about 2%.

7. The material of claim 1, being capable of being formed *in situ* on body tissue or a medical implant by one or both of polymerization and crosslinking.

8. The material of claim 1, adhering to tissue when polymerized thereon.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

9. The material of claim 1, being substantially elastic during a 10% elongation and release therefrom.

10. The material of claim 1, further characterized in being lubricious.

11. The material of claim 1, further characterized in comprising, before polymerization or crosslinking,

a) at least one component which is a macromer of molecular weight of about 1000 Da

or more, at least 20% of the macromer being a hydrophilic block or region and comprising at least one chemically reactive group; and

b) at least one component bearing more than one chemically reactive group.

12. The material of claim 1, further characterized in comprising, before polymerization or crosslinking, at least 20% by weight of at least one amphiphilic water-soluble monomer of molecular weight less than about 1000 Da.

13. The material of claim 1, in which the water absorption at equilibrium hydration is less than about 200%.

14. The material of claim 1, in which the solids content is at least about 25% after equilibrium swelling.

15. The material of claim 1, in which the elongation to failure is at least about 200%.

16. The material of claim 1, in which the tensile modulus is at least 200 kPa.

17. The material of claim 1, further comprising a therapeutic, prophylactic or diagnostic agent.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

18. The material of claim 1 formed by polymerization of a mixture comprising:

a) about 40% to about 100% by weight of one or more polymerizable monomers

having a molecular weight of about 1000 Da or less;

wherein at least about 40% by weight of the monomers consists of amphiphilic monomers;

wherein no more than about 50% by weight of the monomers consists of functionally hydrophobic monomers;

b) 0% to about 40% by weight of a reactive macromer having a molecular weight greater than about 500 Da, which comprises on average more than one polymerizable group per molecule, and which has hydrophilic groups comprising about 20% of the macromer; and

c) 0% to about 40% water.

19. The material of claim 1 in the form of a coating on an implant or device.

20. ~~The material of claim 1 forming an implant or device.~~

A2 21. (Amended) The material of claim 1, further characterized as comprising, before polymerization or crosslinking, a monomer having the formula AHK, wherein:

A is a residue of an ethylenically unsaturated acid that is linked to H by a bond selected from ester and amide;

H is the residue of a hydroxy carboxylic acid, a carbonic acid, or an amino acid, which is linked to K by an ester bond; and

K is the residue of an alcohol containing at least one carbon atom.

22. (Amended) The material of claim 21 wherein

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

A is selected from the group consisting of acrylic, methacrylic crotonic, isocrotonic, tiglic, angelic, and cinnamic acids; maleic, fumaric, citraconic, mesaconic, itaconic, citric and isocitric acids, and monoesters and monoamides thereof, and mixtures thereof;

A2 only
H is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, hydrolyzed dioxanone, a hydroxyhexanoic acid, an alpha, beta or gamma amino acid of eight carbons or fewer, and mixtures thereof; and

K is an alcohol containing from 1 to about 10 carbon atoms and at least one hydroxyl group, or a mixture of such alcohols.

23. (Amended) The material of claim 22 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.

24. (Amended) The material of claim 22 wherein H has one to about eight carbon atoms and is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, and a hydroxyhexanoic acid.

25. (Amended) The material of claim 22 wherein H is selected from the group consisting of hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, and hydrolyzed dioxanone (i.e., 2-hydroxyethoxyacetic acid).

26. (Amended) The material of claim 22 wherein H has two to eight carbon atoms and is selected from the group consisting of an alpha amino acid, a beta amino acid, a gamma amino acid, and mixtures thereof.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

27. (Amended) The material of claim 22 wherein K is selected from the group consisting of methanol, ethanol, propanol, isopropanol, isomers of butanol, isomers of pentanol, and isomers of hexanol.

28. (Amended) An intermediate having the formula AHC wherein A is a residue of an ethylenically unsaturated acid that is linked to H by a bond selected from ester and amide;

H is the residue of a hydroxy carboxylic acid, a carbonic acid, or an amino acid, which is linked to C by an acyl bond; and

C is a leaving group, which is displaced by alcohols to form esters.

29. The intermediate of claim 28, wherein the leaving group C is selected from the group consisting of halogens, succinimidyl group, imidazoles, thiols, nitrophenols, pyridines, and o-acyl ureas.

30. The intermediate of claim 28 wherein A is selected from the group consisting of acrylic, methacrylic crotonic, isocrotonic, tiglic, angelic, and cinnamic acids; maleic, fumaric, citraconic, mesaconic, itaconic, citric and isocitric acids, and monoesters and monoamides thereof; and mixtures thereof.


31. The intermediate of claim 28 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.

32. The intermediate of claim 28 wherein H is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT


carbonic acid, hydrolyzed dioxanone (2-hydroxyethoxy acetic acid), a hydroxyhexanoic acid, an alpha, beta or gamma amino acid of eight carbons or fewer, and mixtures thereof.

33. The material of claim 1, wherein the tissue is orthopedic tissue.

 34. (Amended) The material of claim 33, wherein the tissue is selected from the group consisting of bone, cartilage, meniscus, bursa, synovial membranes, tendons, ligaments, muscle and vertebral disks.

35. The material of claim 1, wherein the material is effective to provide lubricity, abrasion-resistance, load distribution, or resurfacing to an orthopedic tissue.

36. The material of claim 1, wherein the material adheres to tissue.

 37. (Amended) A method for the treatment of biological tissue or a medical implant comprising applying a crosslinked polymeric hydrogel material to the tissue or implant, wherein the material has both hydrophilic and hydrophobic regions and is characterized as having the following properties:

- a) absorbing water to less than about 300% of its initial weight, on exposure to water or bodily liquids;
- b) having a solids content of at least about 20% after equilibration in water or bodily fluids;
- c) having an elongation to failure of at least about 25% both as formed and after swelling to equilibrium; and
- d) being biocompatible;

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

AS
wherein the material is formed by the crosslinking of reactive monomers and macromers
in the presence of tissue, and undergoes hydration with bodily liquids to form a water-containing
material.

AS
38. (New) A composition for forming a water-absorbing, high modulus polymeric
material comprising at least one macromer and at least one monomer,

Sub B1
wherein the macromer comprises hydrophobic and hydrophilic regions and has a
molecular weight of 500 to 200,000 Da,

wherein the monomer contains at least one vinyl group and has a molecular weight of
less than 1,000 Da, and

wherein the monomer comprises at least 30% (wt/wt) of the composition.

39. (New) The composition of claim 38, wherein the composition is in the form of a
fluid or paste.

40. (New) The composition of claim 38, further comprising water.

41. (New) The composition of claim 38, wherein the macromer is
polyethyleneglycol-trimethylene carbonate-diacrylate.

42. (New) The composition of claim 38, wherein the monomer is selected from the
group consisting of vinyl caprolactam, methyl acrylate, methyl methacrylate, styrene, N-vinyl
pyrrolidone, and N-vinyl imidazole, diacetone acrylamide, vinyloxyethanol, 2-acrylamido-2-
methylpropane, and methyl acryloyl lactate and mixtures and derivatives thereof.

43. (New) The composition of claim 38, wherein the macromer comprises up to 50%
(wt/wt) of the formulation and the monomer comprises at least 45% (wt/wt) of the formulation.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

44. (New) The composition of claim 43, further comprising less than 40% (wt/wt) water.

45. (New) The composition of claim 41, wherein the monomer is diacetone acrylamide.

AS
mfdb
46. (New) The composition of claim 38, wherein upon copolymerization of the macromer and monomer, a polymeric material is formed, wherein the material comprises hydrophobic and hydrophilic regions and is characterized as having the following properties:

- a) absorbing water to less than about 300% of its initial weight, on equilibration with water or bodily liquids;
- b) having a solids content of at least about 20% after equilibration in water or bodily liquids;
- c) having an elongation to failure of at least about 25% hydration to equilibrium; and
- d) being sufficiently biocompatible to permit the treatment or repair of biological tissue, or used as an implant in a patient.

47. (New) The composition of claim 38, wherein the macromer has the formula AHK, wherein:

A is a residue of an ethylenically unsaturated acid that is linked to H by a bond selected from ester and amide;

H is the residue of a hydroxy carboxylic acid, a carbonic acid, or an amino acid, which is linked to K by an ester bond; and

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

K is the residue of an alcohol containing at least one carbon atom.

48. (New) The composition of claim 47 wherein

A is selected from the group consisting of acrylic, methacrylic crotonic, isocrotonic, tiglic, angelic, and cinnamic acids; maleic, fumaric, citraconic, mesaconic, itaconic, citric and isocitric acids, and monoesters and monoamides thereof, and mixtures thereof;

H is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, hydrolyzed dioxanone, a hydroxyhexanoic acid, an alpha, beta or gamma amino acid of eight carbons or fewer, and mixtures thereof; and

K is an alcohol containing from 1 to about 10 carbon atoms and at least one hydroxyl group, or a mixture of such alcohols.

49. (New) The composition of claim 48 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.
